## REMARKS

### I. Rejection of Claims 24, 27-29, and 32 Under the Judicially Created Doctrine of Double Patenting over Claims 1-4 of U.S. Patent No. 5, 817,479

The Examiner rejected Claims 24, 27-29, and 32 under the judicially created doctrine of double patenting over Claims 1-4 of U.S. Patent No. 5, 817,479. The Examiner stated that "Claim 1 of '479 claims polynucleotides encoding biologically active fragments and immunogenically active fragments of SEQ ID NO:2 9 [*sic*] and a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:9." (Office Action, page 3.) Amended Claim 24 does not recite "biologically active" fragments or "immunogenic" fragments, and Claim 32 is canceled. Therefore, Applicants respectfully request that the Examiner withdraw the double patenting rejection of Claims 24, 27-29, and 32.

### II. Rejection of Claims 24-32 Under 35 U.S.C. § 112, second paragraph

#### A. Claims 24-32

The Examiner rejected Claims 24-32 under 35 U.S.C. § 112, second paragraph, alleging that the claims were indefinite because they "contain non-elected subject matter and therefore do not particularly point out and distinctly claim the subject matter of the elected invention." (Office Action, page 4.) Solely in order to expedite prosecution, Applicants have amended the claims such that non-elected subject matter is no longer recited. Applicants reserve the right to prosecute the subject matter of non-elected claims, or of any subject matter disclosed but not herein claimed, in a later continuation or divisional application.

#### B. Claim 24

The Examiner rejected Claim 24 under 35 U.S.C. § 112, second paragraph, alleging that the claim was indefinite because it recites "biologically active fragments." (Office Action, page 4.) Solely in order to expedite prosecution, Applicants have amended Claim 24 such that "biologically active fragments" are no longer recited.

**C. Claims 24 and 31**

The Examiner rejected Claims 24 and 31 under 35 U.S.C. § 112, second paragraph, alleging that the claims were indefinite because of the recitation of the phrase "at least 90% identical to." The Examiner suggested the replacement of "identical" with "identity." Accordingly, Applicants have amended Claim 24 to recite "a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2" and Claim 31 to recite "a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:9."

**D. Claims 24 and 27**

The Examiner rejected Claims 24 and 27 under 35 U.S.C. § 112, second paragraph, alleging that the claims were indefinite for depending from unelected claims. Applicants have amended Claim 24 to an independent claim and Claim 27 such that it depends from Claim 24.

**E. Claim 32**

The Examiner rejected Claim 32 under 35 U.S.C. § 112, second paragraph, alleging that Claim 32 "broadens the scope of Claim 31." (Office Action, page 4.) Solely in order to expedite prosecution, Claim 32 has been canceled.

For at least the above reasons, Applicants respectfully request that the Examiner withdraw the rejections under 35 U.S.C. § 112, second paragraph.

**III. Rejection of Claims 24 and 27-32 Under 35 U.S.C. § 112, first paragraph, written description**

Claims 24 and 27-32 were rejected under the first paragraph of 35 U.S.C. 112 for alleged lack of an adequate written description. The Examiner alleged that "[w]ithout a statement regarding the activity of a polynucleotides [*sic*] encoding a polypeptide have [*sic*] 90% identity to SEQ ID NO:2, or biologically active or immunogenically active fragments of SEQ ID NO:2 or of polynucleotides that are 90% identical to SEQ ID NO:9 and encode a polypeptide having no function one skilled in the art

cannot know the metes and bounds of the claimed polynucleotides." (Office Action, page 5.) Solely in order to expedite prosecution, Applicants have amended Claim 24 such that fragments are no longer recited and have canceled Claim 32. Therefore the rejection as it pertains to fragments is moot.

The Examiner ignores the claim limitations of "having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2" and "having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:9," and attempts to introduce a limitation of "function" to the polypeptide variants and polynucleotide variants, limitations which are not present in the pending claims. The Examiner ignores the limitation that the claimed polynucleotides encode a polypeptide comprising a naturally occurring amino acid sequence or comprise a naturally occurring polynucleotide sequence.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

SEQ ID NO:2 and SEQ ID NO:9 are specifically disclosed in the application (see, for example, pages 61-62 and 68-69). Variants of SEQ ID NO:2 are described, for example, at page 16, lines 19-27. In particular, the preferred, more preferred, and most preferred SEQ ID NO:2 variants (80%, 90%, and 95% amino acid sequence similarity to SEQ ID NO:2) are described, for example, at page 21, lines 2-6. Incyte clones in which the nucleic acids encoding the human DAPK-2 were first identified and libraries from which those clones were isolated are described, for example, at page 18, lines 3-7 of the Specification. Chemical and structural features of DAPK-2 are described, for example, on page 18, lines 8-14. Given SEQ ID NO:2, one of ordinary skill in the art would recognize "a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2." Given SEQ ID NO:9, one of ordinary skill in the art would recognize "a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:9." The Specification describes (e.g., page 50, line 30 through page 51, line 25) how to use BLAST to determine whether a given sequence falls within the "having at least 90% sequence identity" scope.

There simply is no requirement that the claims recite particular variant polypeptide or polynucleotide sequences because the claims already provide sufficient structural definition of the claimed subject matter. That is, the polypeptide variants are defined in terms of SEQ ID NO:2 ("An isolated polynucleotide encoding a polypeptide selected from the group consisting of. .b) a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2." The polynucleotide variants are defined in terms of SEQ ID NO:9 ("An isolated polynucleotide selected from the group consisting of . . . b) a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:9.")

Because the recited polypeptide variants are defined in terms of SEQ ID NO:2, and the recited polynucleotide variants are defined in terms of SEQ ID NO:2 and SEQ ID NO:9, the precise chemical structure of every polypeptide variant and every polynucleotide fragment within the scope of the claims can be discerned. The Examiner's position is nothing more than a misguided attempt to require

Applicants to unduly limit the scope of their claimed invention. Accordingly, the Specification provides an adequate written description of the recited polypeptide and polynucleotide sequences.

### A. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides and polypeptides in terms of chemical structure, rather than on functional characteristics. For example, the "variant language" of independent claims 24 and 31 recites chemical structure to define the claimed genus:

> 24. An isolated polynucleotide encoding a polypeptide selected from the group consisting of. . . :
>
> b) a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2.
>
> 31. An isolated polynucleotide selected from the group consisting of . . . :
>
> b) a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:9 . .

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO: 2 and SEQ ID NO:9. In the present case, there is no reliance merely on a description of functional characteristics of the polynucleotides or polypeptides recited by the claims. In fact, there is no recitation of functional

characteristics. Moreover, if such functional recitations were included, it would add to the structural characterization of the recited polynucleotides or polypeptides. The polynucleotides or polypeptides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

**B. The present claims do not define a genus which is "highly variant"**

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant." Available evidence illustrates that the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078) (Reference No. 1). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

The present application is directed, *inter alia*, to disease associated protein kinases related to the amino acid sequence of SEQ ID NO:2. In accordance with Brenner et al, naturally occurring molecules may exist which could be characterized as disease associated protein kinases and which have as little as 40% identity over at least 70 residues to SEQ ID NO:2. The "variant language" of the present claims recites, for example, polynucleotides encoding "a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2" (note that SEQ ID NO:2 has 448 amino acid residues). This variation is far less than

that of all potential disease associated protein kinases related to SEQ ID NO:2, i.e., those disease associated protein kinases having as little as 40% identity over at least 70 residues to SEQ ID NO:2.

### C. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those case was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of June 19, 1997. Much has happened in the development of recombinant DNA technology in the 17 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:2 and SEQ ID NO:9, and the additional extensive detail provided by the subject application, the present inventors were in possession of the recited polypeptide variants and polynucleotide variants at the time of filing of this application.

### D. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical

structure of SEQ ID NO:2 or SEQ ID NO:9. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides or polypeptides defined by the present claims is adequately described, as evidenced by Brenner et al. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

## IV. Rejection of Claims 24, 27-29, and 32 Under 35 U.S.C. § 102(e) as Being Anticipated by Au-Young et al.

The Examiner rejected Claims 24, 27-29, and 32 under 35 U.S.C. § 102(e) as being anticipated by Au-Young et al. (USP 5,817,479). The Examiner stated that "Claim 1 of '479 claims polynucleotides encoding biologically active fragments and immunogenically active fragments of SEQ ID NO:2 9 [*sic*] and a polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO:9." (Office Action, page 6.) Amended Claim 24 does not recite "biologically active" fragments or "immunogenic" fragments, and Claim 32 is canceled. The Au-Young et al. document does not anticipate the claims, and therefore Applicants respectfully request that the Examiner withdraw the prior art rejection over Au-Young et al.

## V. Rejection of Claims 24, 27, 28, and 32 Under 35 U.S.C. § 102(a) as Being Anticipated by Hillier et al.

The Examiner rejected Claims 24, 27, 28, and 32 under 35 U.S.C. § 102(a) as being anticipated by Hillier et al. The Examiner stated that "Hillier et al. teach a polynucleotide encoding biologically active fragments and immunogenically active fragments of SEQ ID NO:2 (Claim 24)" and that "[t]his polynucleotide comprises at least 60 contiguous nucleotides of SEQ ID NO:9 (Claim 32)." (Office Action, pages 6-7.) Amended Claim 24 does not recite "biologically active" fragments or "immunogenic" fragments, and Claim 32 is canceled. The Hillier et al. document does not anticipate the claims, and therefore Applicants respectfully request that the Examiner withdraw the prior art rejection over Hillier et al.

## VI. Rejection of Claims 24 and 32 Under 35 U.S.C. § 102(b) as Being Anticipated by Myers

The Examiner rejected Claims 24 and 32 under 35 U.S.C. § 102(b) as being anticipated by Myers. The Examiner stated that "Myer [*sic*] teaches a polynucleotide encoding biologically active fragments and immunogenically active fragments of SEQ ID NO:2 (Claim 24)" and that "[t]his polynucleotide comprises at least 60 contiguous nucleotides of SEQ ID NO:9." (Office Action, page 7.) Amended Claim 24 does not recite "biologically active" fragments or "immunogenic" fragments, and Claim 32 is canceled. The Myers document does not anticipate the claims, and therefore Applicants respectfully request that the Examiner withdraw the prior art rejection over Myers.

## VII. Rejection of Claims 24, 27-29, and 32 Under 35 U.S.C. § 102(e) as Being Anticipated by Nezu et al.

The Examiner rejected Claims 24, 27-29, and 32 under 35 U.S.C. § 102(e) "as being anticipated by Nezu et al. (USP 6,265,194, priority to December 1997)." (Office Action, page 7.) The instant application claims priority to U.S. Application Serial No. 08/878,989, filed June 19, 1997 (acknowledged by the Examiner on page 2 of the Office Action) and therefore has an effective filing date of June 19, 1997. The Nezu et al. document has June 25, 1999 as its effective date as a reference under 35 U.S.C. §102(e). See MPEP 2136.03 below.

> CONTINUATION OF AN INTERNATIONAL (PCT) APPLICATION; INTERNATIONAL APPLICATION PUBLICATION
>
> A patent issued from a U.S. application filed under 35 U.S.C. 111(a) that claims the benefit of the filing date of a copending PCT international application under 35 U.S.C. 120, has as its effective date as a reference under 35 U.S.C. 102(e) the U.S. filing date of the 35 U.S.C. 111(a) application and not the international filing date. This is true whether the application being examined is a pre PG-PUB application or a PG-PUB application (see MPEP § 2136). (MPEP 2136.03.)

Therefore, the Nezu et al. document is not 35 U.S.C. § 102(e) prior art against the instant application. Applicants respectfully request that the Examiner withdraw the prior art rejection over Nezu et al.

## CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent at (650) 845-4646.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: February 3, 2003

Susan K. Sather

Susan K. Sather
Reg. No. 44,316
Direct Dial Telephone: (650) 845-4646

3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

## IN THE CLAIMS:

Claim 32 has been canceled.

Claims 24, 25, 26, 27, 29, 30, and 31 have been amended as follows:

24. (Once Amended) An isolated polynucleotide encoding a polypeptide [of claim 22] selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence of SEQ ID NO:2, and

b) a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2.

25. (Once Amended) An isolated polynucleotide encoding a polypeptide [of claim 23] comprising an amino acid sequence of SEQ ID NO:2.

26. (Once Amended) An isolated polynucleotide of claim 25 comprising a polynucleotide sequence [selected from the group consisting] of SEQ ID NO:9 [SEQ ID NO:8-14].

27. (Once Amended) A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 24 [22].

29. (Once Amended) A method of producing a polypeptide selected from the group consisting of a polypeptide comprising an amino acid sequence of SEQ ID NO:2 and a polypeptide comprising a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence of SEQ ID NO:2 [of claim 22], the method comprising:

a) culturing the cell of claim 28 [a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and

said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 22], and

b) recovering the polypeptide so expressed.

30. (Once Amended) A method of claim 29, wherein the polypeptide comprises an amino acid sequence [selected from the group consisting] of SEQ ID NO:2 [SEQ ID NO:1-7].

31. (Once Amended) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence [selected from the group consisting] of SEQ ID NO:9 [SEQ ID NO:8-14],

b) a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity [identical] to a polynucleotide sequence [selected from the group consisting] of SEQ ID NO:9 [SEQ ID NO:8-14],

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).